LEAD EXPOSURE ALTERS NEURAL MECHANISMS OF LEARNING: A PILOT STUDY OF FEAR-POTENTIATED STARTLE IN ELDERLY MEN

Rachel Grashow, *Harvard School of Public Health, Boston, USA*
Linda H. Nie, *School of Health Science, Purdue University, West Lafayette, USA*
David Sparrow, *VA Boston Healthcare System, Boston, USA*
Howard Hu, *University of Michigan School of Public Health, Ann Arbor, USA*
Marc Weisskopf, *Harvard School of Public Health, Boston, USA*

Background and Aims: Physiologically-based indicators of neurological function could provide mechanistic insight into toxicant actions on the brain, and perhaps prove a more objective and sensitive measure of such effects than other methods. We explored the effects of lead exposure on classical conditioning of the acoustic startle reflex (ASR)—a simple form of learning in the brain—in a population of elderly men.

Methods: Fifty-one men from the Normative Aging Study (NAS) with patella and tibia bone lead measurements made with K-X-Ray-Fluorescence participated in a fear-conditioning protocol. One of two visual conditioned stimuli (CS) on a computer was paired with a mild finger shock. Eye-blink responses (electromyogram) to a loud noise burst were recorded with surface electrodes. Conditioning was indexed as the difference in z-scored eye-blink responses to noise bursts delivered in the presence of the paired and non-paired CS after the pairing process—when no shocks were delivered.

Results: The mean age of the men was 76 years (standard deviation [sd]=5.9) and mean patella lead concentration was 22.4µg/g bone (sd=12.2; range=5-63). In unadjusted analyses among 37 men with valid eyeblink responses at the end of the protocol, conditioning was 0.56sd less (95% CI:-1.02, -0.11; p=0.02) per 20 µg/g patella lead (the interquartile range of the parent NAS population). Tibia results were similar. Adjusting for age weakened associations only slightly, but there was no association between age itself and conditioning. Baseline startle amplitude was associated with age (β=-26.577µV per year; 95% CI:-47.67, -5.48; p=0.0137), but not with conditioning.

Conclusions: In elderly men patella bone lead concentrations, a marker of cumulative lead exposure, predicted learning in a fear-conditioning startle paradigm. While the data are taken from a relatively small sample, this initial exploration offers the possibility that the ASR may provide a new paradigm to explore the effects of neurotoxicant exposure.